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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/682,199
Filing Date: October 10, 2003
Appellant(s): HERMENTIN ET AL.

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For Appellant

EXAMINER'S ANSWER

This is in response to the Appeal Brief filed August 10, 2007, appealing from the Office action mailed November 29, 2006.

(1) Real Party in Interest

The Appeal Brief identifies "CSL Behring GmbH" as the Real Party in interest.

(2) Related Appeals and Interferences

Examiner is not aware of any related appeals, interferences, or judicial proceedings affecting, directly affected by, or having a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The Appeal Brief correctly identifies claims 16-25, 27, 28, 30, 31, 33 and 25 under appeal.

(4) Status of Amendments After Final

The Appeal Brief identifies Appellants' amendment after final rejection filed February 22, 2007, which was entered March 21, 2007.

(5) Summary of Claimed Subject Matter

The Appeal Brief correctly summarizes the claimed subject matter.

(6) Grounds of Rejection to be Reviewed on Appeal

The Appeal Brief correctly identifies the rejections to be reviewed on appeal.

(7) Claims Appendix

The copy of the appealed claims in the Claims Appendix to the Appeal Brief is correct.

(8) Evidence Relied Upon

Shainoff, J.R. *Electrophoresis and Direct Immunoprobing on Glyoxyl Agarose and Polyacrylamide Composites*, in ADVANCES IN ELECTROPHORESIS, Chrambach, Dunn & Radola, Eds., VCH Publishers, New York, Vol. 6, pp. 65-176 (1993).

Bhat, S.P. & Nagineni, C.N. Use of "Submarine" Gel Electrophoresis for Running Multiple Two-Dimensional Protein Gels. ANAL. BIOCHEM. 1988;170:105-109.

Perrella, M. & Denisov, I. Low-Temperature Electrophoresis Methods. METHODS ENZYMOL. 1995;259:468-487.

(9) Grounds of Rejection

The following grounds of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness[1,2] rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 16-24, 27-28, 30-31, 33 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shainoff, *Electrophoresis and direct immunoprobing on glyoxal agarose*, in ADVANCES IN ELECTROPHORESIS, Vol. 6, VCH Publishers, pp. 65-176 (1993), in view of Bhat & Nagineni, 170 ANAL. BIOCHEM 105 (1988).

Shainoff teaches a method for the determination of multimers of multimer-forming proteins by gel electrophoresis, comprising:

> fractionating a sample containing von Willebrand factor[3] or fibrinogen[4] into multimer bands by electrophoresis using a continuous,[5] homogeneous[6] agarose gel;[7]

[1] In the Supreme Court decision *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), the Court set forth factual inquiries establishing a background for determining obviousness under 35 U.S.C. 103(a). The factual inquiries include: (1) determining the scope and contents of the prior art; (2) ascertaining the differences between the prior art and the claims at issue; (3) resolving the level of ordinary skill in the pertinent art; and (4) considering objective evidence indicating obviousness or nonobviousness.

visualizing multimer bands by a dye in the gel;[8]

optionally, quantifying the dyed multimer bands.[9]

Shainoff does not describe "submarine" electrophoresis.

However, Bhat & Nagineni describe the use of "submarine" electrophoresis for resolving proteins (see Title).

It would have been obvious for a person of ordinary skill in the art to replace the electrophoretic protocol of Shainoff with a "submarine" method because Bhat & Nagineni discovered that the "submarine" method allows for stacking of multiple gels allowing for multiple simultaneous runs (see Abstract).

With respect to 1) and 3), Shainoff describes gels made of either "agarose" or "glyoxal agarose", or both. For example, Shainoff experimented with gels made of "regular agarose" (see p. 67, line 14, "regular agarose"). In addition, Shainoff experimented with "composite gels" made with regular agarose (see p. 72, lines 5-6 of the third paragraph, "composite of glyoxyl agarose with[...] blended with regular agarose") (paraphrasing mine).

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[2] The lack of objective evidence of nonobviousness in the instant application does not suggest "the level of ordinary skill in the pertinent art" is high.
[3] See p. 78, Section *2.1.1.1 Gel concentrations*, first paragraph, line 5, "separating von Willebrand factor multimers".
[4] See p. 66, Section *1.1 Development of glyoxyl agarose and composites*, first paragraph, first sentence, "fibrinogen derivatives".
[5] See Table 1 on p. 75.
[6] *Id.* Examiner equates the term "homogeneous" to the anteceding term "continuous".
[7] See *e.g.*, Title; see *also*, p. 67, line 14, "regular agarose"; see *also*, p. 72, lines 5-6 of the third paragraph, "composite of glyoxyl agarose with[...] blended with regular agarose"; see also, p. 74, first paragraph, last sentence, "Our focus in this work is on agarose gels with the low sieving characteristics of regular agarose, and composites").
[8] See p. 98, left column, Section *2.7 General protein staining*.
[9] See p. 99, Section *2.8 Mounting, photographing and scanning gels*, first paragraph, second sentence, "densitometers".

Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Shainoff, *Electrophoresis and direct immunoprobing on glyoxal agarose*, in ADVANCES IN ELECTROPHORESIS, Vol. 6, VCH Publishers, pp. 65-176 (1993), and Bhat & Nagineni, 170 ANAL. BIOCHEM 105 (1988), as applied to claim 16 and 24, and further in view of Perrella & Denisov, 259 METHODS ENZYMOL. 468 (1995).

Shainoff and Bhat & Nagineni describe a method for the determination of multimers as substantially described, *supra*, and incorporated herein.

Shainoff and Bhat & Nagineni do not describe a method wherein electrophoresis is carried out between 8-12°C.

However, Perrella & Denisov describe the use of temperature to modify electrophoresis (see Title).

It would have been obvious for a person of ordinary skill in the art to modifty the electrophoretic protocol of Shainoff and Bhat & Nagineni by modifying temperature because Perrella & Denisov teach that the use of temperature to modify electrophoresis allows for probing of "intermediate stages of ligation" and "quaternary structural changes" (see first paragraph).

(10) Response to Argument

Appellants argue:

1. Shainoff describes immunoperoxidase-stained fibrinogen ran on glyoxal agarose in Figure 4, which is different than Appellants' claimed dye-stained fibrinogen ran on agarose (see Appeal Brief, p. 9, first and second full paragraphs).

2. Shainoff do not teach the claimed invention because Shainoff is a general review article teaching different electrophoresis procedures using different gels and different gel stains, which are not linked to point out the method recited in claim 16 (see Appeal Brief, paragraph bridging pp. 9-10 to p. 10, second full paragraph; see *also*, paragraph briding pp. 11-12).

3. The cited prior art provide no motivation to use Appellants' inferior dye labels in inferior continuous gels (see Appeal Brief, p. 10, second full paragraph to p. 11, first full paragraph; see *also*, p. 12, first full paragraph).

4. Bhat & Nagineni describe an entirely different electrophoresis procedure than Appellants' claimed procedure (see Appeal Brief, p. 13, first paragraph).

5. Perrella & Denisov describe an electrophoresis procedure specifically tailored to hemoglobin and do not suggest the precise temperature range of claim 25 (see Appeal Brief, Section III).

Appellants' arguments are not persuasive.

With respect to arguments 1) and 2), Examiner acknowledges that Shainoff describes immunoperoxidase-stained fibrinogen ran on glyoxal agarose in Figure 4, which is different than Appellants' claimed dye-stained fibrinogen ran on agarose, which Shainoff also teaches can be dye-stained[10] and ran on agarose.[11] Furthermore, Examiner observes that Shainoff teaches all these things in ONE concise journal article, so there is no need for pointing out Shainoff's concepts and calling them a "disparate".

With respect to argument 3), Examiner is unable to locate any objective evidence from Shainoff or Bhat & Nagineni that either Shainoff or Bhat & Nagineni share Appellants' bias against dye labels and continuous gels. To the contrary, Shainoff appears to endorse both dye labels and continuous gels by describing them in his journal article in an objective, unbiased manner as viable alternatives to fractionating either von Willebrand factor[12] or fibrinogen.[13]

With respect to argument 4), the test for obviousness is not whether the structural features of either Shainoff or Bhat & Nagineni may be bodily incorporated into Applicants' invention. Rather, the test is whether the combined teachings of Shainoff or Bhat & Nagineni suggest Applicants' invention. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). One cannot show nonobviousness by attacking the teachings of Shainoff and Bhat & Nagineni individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

With respect to argument 5), Examiner respectfully disagrees with Appellants' position that application of Perrella's & Denisov's procedure is limited to hemoglobin. In addition to hemoglobin, Perrella & Denisov appear to suggest their technique is applicable to other multimeric proteins.[14] Thus, persons of ordinary skill practicing Shainoff's and Bhat's electrophoresis method may find motivation to lower the electrophoresis temperature because Perrella & Denisov demonstrated the ability of lower temperatures to capture "intermediate stages of ligation" and "quaternary structural changes"[15] of a multimeric protein. With respect to the precise temperature range of claim 25, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. See *In re Aller,* 105 USPQ 233 (CCPA 1955).

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[10] See *supra*, note 8.
[11] See *supra*, note 7.
[12] See *supra*, note 3.
[13] See *supra*, note 4.
[14] See p. 470, first full paragraph, "Although the techniques of cryogenic quenching for the stabilization of reaction intermediates and cryogenic electrophoresis for the separation of such intermediates may find application to the study of other proteins, our experience has been limited to the study of the hemoglobin reactions."
[15] See first paragraph.

(11) Related Proceeding(s) Appendix

Examiner is not aware of any related appeals, interferences, or judicial proceedings affecting, directly affected by, or having a bearing on the Board's decision in the pending appeal.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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